

10/520,066

=> file casreact

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FILE CONTENT:1840 - 11 Dec 2005 VOL 143 ISS 24

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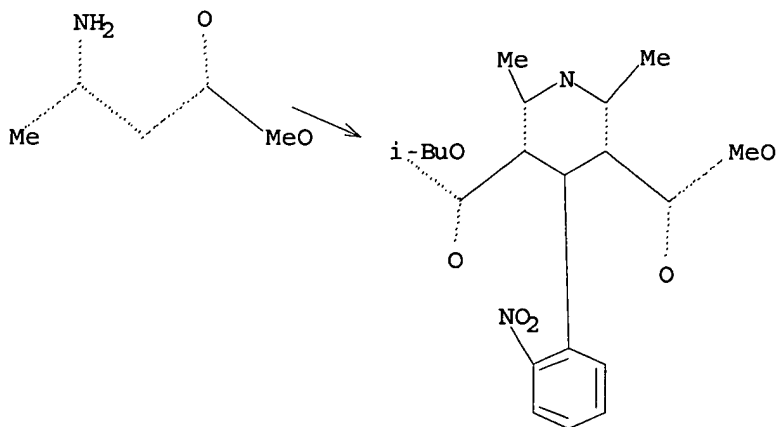
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This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d que

L1 STR



Structure attributes must be viewed using STN Express query preparation.

L3 3 SEA FILE=CASREACT SSS FUL L1 ( 9 REACTIONS)

=> d l3 1-3 ibib abs fcrd

L3 ANSWER 1 OF 3 CASREACT COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 143:367186 CASREACT

TITLE: Study on synthesis of 1,4-dihydro-2,6-dimethyl-4-(3-nitrophenyl)-3,5-pyridinedicarboxylic acid isobutyl methyl ester

AUTHOR(S): Chen, Yaping; Yu, Bin

CORPORATE SOURCE: Department of Chemical Technology, Jiang Yin Vocational College, Jiangyin, 214433, Peop. Rep. China

SOURCE: Wuxi Qinggong Daxue Xuebao (2003), 22(4), 57-59, 68

10/520,066

CODEN: WQDXF3; ISSN: 1009-038X

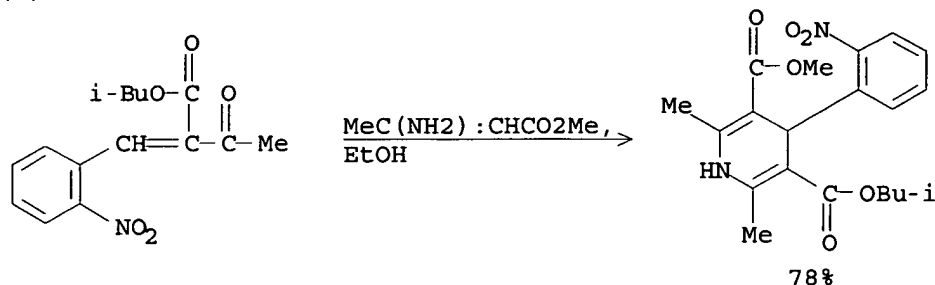
PUBLISHER: Wuxi Qinggong Daxue Xuebao Bianjibu

DOCUMENT TYPE: Journal

LANGUAGE: Chinese

AB An improved three-steps method for synthesis of 1,4-dihydro-2,6-dimethyl-4-(2-nitrophenyl)-3,5-pyridinedicarboxylic acid iso-Bu Me ester with anti-hypertension activity was reported. The process has the advantage of short reaction time, and improved yield. The structure of the final product was confirmed by elemental anal., IR, <sup>1</sup>H NMR and <sup>13</sup>C NMR.

RX(3) OF 6



CON: room temperature -> reflux

L3 ANSWER 2 OF 3 CASREACT COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 140:77036 CASREACT

TITLE: Industrial production process for the synthesis of isobutyl methyl 1,4-dihydro-2,6-dimethyl-4-(2-nitrophenyl)-3,5-pyridine dicarboxylate (nisoldipine)  
INVENTOR(S): Ferrari, Massimo; Ghezzi, Marcello; Alberelli, Manuel; Ambrosini, Alberto

PATENT ASSIGNEE(S): Erregierre S.p.A., Italy

SOURCE: PCT Int. Appl., 10 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

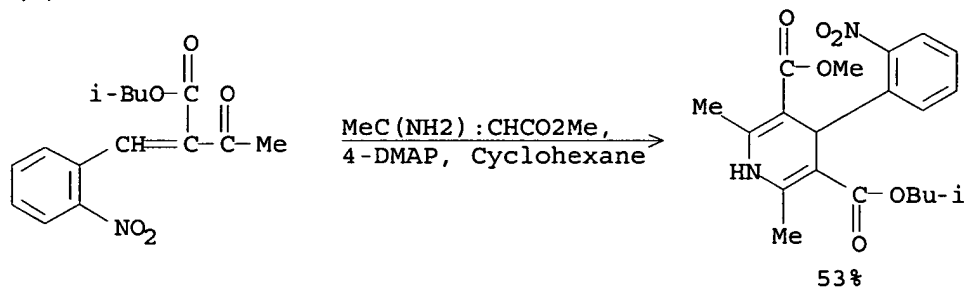
| PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE     |
|---|------|----------|-----------------|----------|
| WO 2004002958   | A1   | 20040108 | WO 2003-EP6755  | 20030626 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW |      |          |                 |          |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG  |      |          |                 |          |
| EP 1532110  | A1   | 20050525 | EP 2003-761517  | 20030626 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK   |      |          |                 |          |
| US 2005240022   | A1   | 20051027 | US 2005-520066  | 20050103 |
| PRIORITY APPLN. INFO.: IT 2002-MI1445 20020701  |      |          |                 |          |
| WO 2003-EP6755 20030626   |      |          |                 |          |

AB The process of iso-Bu Me 1,4-dihydro-2,6-dimethyl-4-(2-nitrophenyl)-3,5-pyridine dicarboxylate (Nisoldipine) synthesis is by the reaction of

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iso-Bu 2-(2-nitrobenzylidene)acetoacetate with Me 3-aminocrotonate in an apolar solvent, added to the reaction mixture in a single portion or portionwise in an apolar solvent, to give crude Nisoldipine, purified by crystallization from a water/water soluble solvent mixture such as water/acetone mixture

RX(2) OF 3



NOTE: work up

CON: STAGE(1) 10 hours, reflux; 16 hours, reflux

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 3 CASREACT COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 112:138871 CASREACT

TITLE: Syntheses of [4-carbon-14]- and [6-carbon-14]nisoldipine

AUTHOR(S): Scherling, D.; Pleiss, U.

CORPORATE SOURCE: Inst. Pharmacokinet., Bayer A.-G., Wuppertal, D-5600, Fed. Rep. Ger.

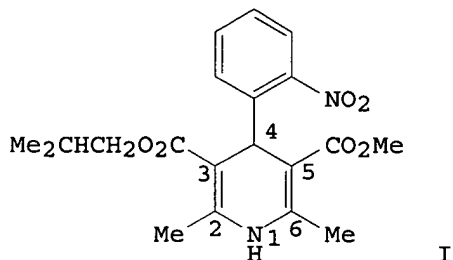
SOURCE: Journal of Labelled Compounds and Radiopharmaceuticals (1988), 25(12), 1393-400

CODEN: JLCRD4; ISSN: 0362-4803

DOCUMENT TYPE: Journal

LANGUAGE: English

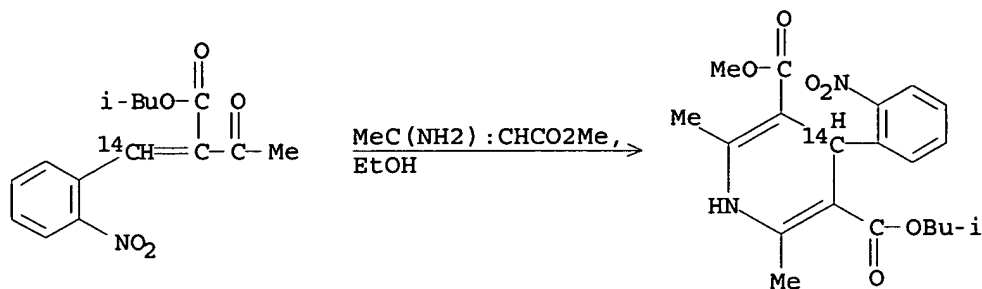
GI



AB The synthesis of [4-<sup>14</sup>C]nisoldipine I starting from di-Me [<sup>14</sup>C]formamide (II) was described. II reacts with 2-O<sub>2</sub>NC<sub>6</sub>H<sub>4</sub>Li yielding 2-nitro[7-<sup>14</sup>C]benzaldehyde which on Knoevenagel condensation with iso-Bu acetoacetate yielded iso-Bu 2-(2-nitro[7-<sup>14</sup>C]benzylidene)acetoacetate (III). Key reaction step was the cyclizing Michael addition III with Me 3-aminocrotonate to give I.

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RX(3) OF 27



NOTE: In dark

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FILE COVERS 1907 - 13 Dec 2005 VOL 143 ISS 25

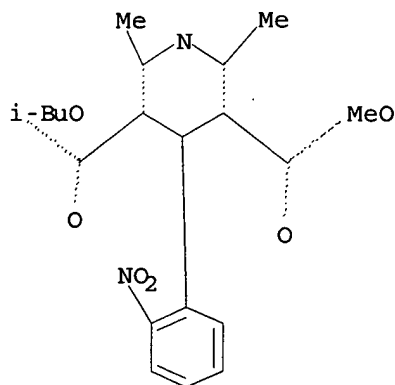
FILE LAST UPDATED: 12 Dec 2005 (20051212/ED)

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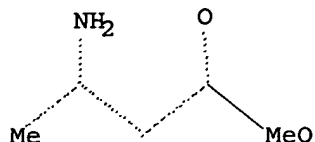
L4 STR



Structure attributes must be viewed using STN Express query preparation.

10/520,066

L5 STR



Structure attributes must be viewed using STN Express query preparation.

L6 21 SEA FILE=REGISTRY SSS FUL L4

L7 315 SEA FILE=REGISTRY SSS FUL L5

L9 11 SEA FILE=CAPLUS L6 AND L7

=> d 19 1-11 ibib abs hit

L9 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:1065302 CAPLUS

DOCUMENT NUMBER: 143:367186

TITLE: Study on synthesis of 1,4-dihydro-2,6-dimethyl-4-(3-nitrophenyl)-3,5-pyridinedicarboxylic acid isobutyl methyl ester

AUTHOR(S): Chen, Yaping; Yu, Bin

CORPORATE SOURCE: Department of Chemical Technology, Jiang Yin Vocational College, Jiangyin, 214433, Peop. Rep. China

SOURCE: Wuxi Qinggong Daxue Xuebao (2003), 22(4), 57-59, 68  
CODEN: WQDXF3; ISSN: 1009-038X

PUBLISHER: Wuxi Qinggong Daxue Xuebao Bianjibu

DOCUMENT TYPE: Journal

LANGUAGE: Chinese

OTHER SOURCE(S): CASREACT 143:367186

AB An improved three-steps method for synthesis of 1,4-dihydro-2,6-dimethyl-4-(2-nitrophenyl)-3,5-pyridinedicarboxylic acid iso-Bu Me ester with anti-hypertension activity was reported. The process has the advantage of short reaction time, and improved yield. The structure of the final product was confirmed by elemental anal., IR, <sup>1</sup>H NMR and <sup>13</sup>C NMR.

IT 14205-39-1P 61312-59-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(synthesis of dihydrodimethyl(nitrophenyl)-pyridinedicarboxylic acid iso-Bu Me ester)

IT 63675-72-9P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(synthesis of dihydrodimethyl(nitrophenyl)-pyridinedicarboxylic acid iso-Bu Me ester)

L9 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:20659 CAPLUS

DOCUMENT NUMBER: 140:77036

TITLE: Industrial production process for the synthesis of isobutyl methyl 1,4-dihydro-2,6-dimethyl-4-(2-nitrophenyl)-3,5-pyridine dicarboxylate (nisoldipine)  
INVENTOR(S): Ferrari, Massimo; Ghezzi, Marcello; Alberelli, Manuel; Ambrosini, Alberto  
PATENT ASSIGNEE(S): Erregierre S.p.A., Italy  
SOURCE: PCT Int. Appl., 10 pp.  
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE       |
|---|------|----------|-----------------|------------|
| WO 2004002958   | A1   | 20040108 | WO 2003-EP6755  | 20030626   |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW<br>RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG |      |          |                 |            |
| EP 1532110  | A1   | 20050525 | EP 2003-761517  | 20030626   |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK   |      |          |                 |            |
| US 2005240022   | A1   | 20051027 | US 2005-520066  | 20050103   |
| PRIORITY APPLN. INFO.:  |      |          | IT 2002-MI1445  | A 20020701 |
|   |      |          | WO 2003-EP6755  | W 20030626 |
| OTHER SOURCE(S): CASREACT 140:77036   |      |          |                 |            |
| AB The process of iso-Bu Me 1,4-dihydro-2,6-dimethyl-4-(2-nitrophenyl)-3,5-pyridine dicarboxylate (Nisoldipine) synthesis is by the reaction of iso-Bu 2-(2-nitrobenzylidene)acetoacetate with Me 3-aminocrotonate in an apolar solvent, added to the reaction mixture in a single portion or portionwise in an apolar solvent, to give crude Nisoldipine, purified by crystallization from a water/water soluble solvent mixture such as water/acetone mixture   |      |          |                 |            |
| REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT   |      |          |                 |            |
| IT 552-89-6, 2-Nitrobenzaldehyde 7779-75-1, Isobutyl acetoacetate 14205-39-1, Methyl 3-aminocrotonate<br>RL: RCT (Reactant); RACT (Reactant or reagent)<br>(synthesis of nisoldipine by the reaction of iso-Bu 2-(2-nitrobenzylidene)acetoacetate with Me 3-aminocrotonate)   |      |          |                 |            |
| IT 63675-72-9P, Nisoldipine<br>RL: IMF (Industrial manufacture); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)<br>(synthesis, by the reaction of iso-Bu 2-(2-nitrobenzylidene)acetoacetate with Me 3-aminocrotonate)  |      |          |                 |            |
| L9 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN  |      |          |                 |            |
| ACCESSION NUMBER: 2000:573777 CAPLUS  |      |          |                 |            |
| DOCUMENT NUMBER: 133:177100   |      |          |                 |            |
| TITLE: Preparation of unsymmetrical 4-aryl-1,4-dihydropyridine-3,5-dicarboxylates from phenylbisbenzylidenemethylenediamines, ketoesters, and aminocrotonates.  |      |          |                 |            |
| INVENTOR(S): Bozsing, Daniel; Kovanyine Lax, Gyorgyi; Simig, Gyula; Tompe, Peter; Blasko, Gabor   |      |          |                 |            |
| PATENT ASSIGNEE(S): Egis Gyogyszergyar Rt., Hung.   |      |          |                 |            |
| SOURCE: PCT Int. Appl., 27 pp.<br>CODEN: PIXXD2   |      |          |                 |            |
| DOCUMENT TYPE: Patent   |      |          |                 |            |
| LANGUAGE: English   |      |          |                 |            |
| FAMILY ACC. NUM. COUNT: 1   |      |          |                 |            |
| PATENT INFORMATION:   |      |          |                 |            |

| PATENT NO.   | KIND | DATE     | APPLICATION NO. | DATE     |
|--|------|----------|-----------------|----------|
| WO 2000047560  | A2   | 20000817 | WO 2000-HU12    | 20000215 |
| WO 2000047560  | A3   | 20001102 |                 |          |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, |      |          |                 |          |

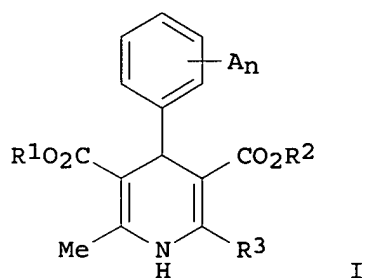
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CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, ID, IL, IN,  
IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD,  
MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK,  
SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ,  
BY, KG, KZ, MD, RU, TJ, TM  
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,  
DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,  
CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: HU 1999-353 A 19990215

OTHER SOURCE(S): CASREACT 133:177100; MARPAT 133:177100

GI



AB Title compds. (I; R1, R2 = alkyl, methoxyethyl, cyanoethyl; R1 and R2 are different; R3 = alkyl, hydroxyalkyl, haloalkyl, PhCH2OCH2, CH2OCH2CH2X; X = halo, N3, NR4R5; R4, R5 = H, alkyl; R4R5N = phthaloyl; A = NO2, halo; n = 1, 2) were prepared by (a) reaction of (II; A, n as above) with R1O2CH2C(OMe) and R2O2CCH:C(NH2)R3 (R1-R3 as above); or (b) reaction of II with R2O2CH2COR3 and R1O2CH:C(NH2)Me (R1-R3 as above) and if desired further transformations of I into other I. Thus, 1-(3-nitrophenyl)-N,N'-bis(3-nitrobenzylidene)methylenediamine, Me 3-aminocrotonate, and Et acetoacetate were refluxed 15 h in isopropanol to give 86% 3-ethyl-5-methyl-2,6-dimethyl-4-(3-nitrophenyl)-1,4-dihydropyridine-3,5-dicarboxylate (nitrendipin).

IT 63675-72-9P 79781-21-8P 88150-62-3P 107812-86-2P  
221446-45-3P 288254-53-5P

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(preparation of asym. 4-aryl-1,4-dihydropyridine-3,5-dicarboxylates from phenylbisbenzylidenemethylenediamines, ketoesters, and aminocrotonates)

IT 105-45-3, Methyl acetoacetate 141-97-9, Ethyl acetoacetate 638-07-3,  
Ethyl 4-chloroacetoacetate 1498-93-7 6334-18-5, 2,3-Dichlorobenzaldehyde 7318-00-5, Ethyl 3-aminocrotonate  
14205-39-1, Methyl 3-aminocrotonate 39562-70-4 51625-68-4  
67354-34-1, Ethyl 4-benzyloxyacetoacetate 85518-49-6, Ethyl  
4-hydroxyacetoacetate 88150-75-8 126192-88-9 130000-32-7,  
2-Methylpropyl acetoacetate 288254-56-8

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of asym. 4-aryl-1,4-dihydropyridine-3,5-dicarboxylates from phenylbisbenzylidenemethylenediamines, ketoesters, and aminocrotonates)

L9 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:271337 CAPLUS

DOCUMENT NUMBER: 130:296614

TITLE: Pyridyl compounds and pharmaceutical compositions containing them

INVENTOR(S): Statkow, Pierre; Straumann, Danielle; Chatterjee, Shyam S.; Sunkel Letelier, Carlos; Fau De Casa-Juana

Munoz, Miguel; Alvarez-Builla, Gomez Julio; Minguez  
Ortega, Jose M.  
PATENT ASSIGNEE(S): Cermol S.A., Switz.  
SOURCE: PCT Int. Appl., 48 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

| PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE       |
|---|------|----------|-----------------|------------|
| WO 9919302  | A1   | 19990422 | WO 1998-IB1555  | 19981007   |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |      |          |                 |            |
| RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG  |      |          |                 |            |
| CH 692199   | A    | 20020315 | CH 1997-2364    | 19971009   |
| CH 692199   | A8   | 20020614 |                 |            |
| CA 2306789  | AA   | 19990422 | CA 1998-2306789 | 19981007   |
| AU 9892771  | A1   | 19990503 | AU 1998-92771   | 19981007   |
| AU 747150   | B2   | 20020509 |                 |            |
| EP 1023267  | A1   | 20000802 | EP 1998-945453  | 19981007   |
| EP 1023267  | B1   | 20030917 |                 |            |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI   |      |          |                 |            |
| JP 2001519415   | T2   | 20011023 | JP 2000-515875  | 19981007   |
| AT 250034   | E    | 20031015 | AT 1998-945453  | 19981007   |
| PT 1023267  | T    | 20040130 | PT 1998-945453  | 19981007   |
| ES 2206989  | T3   | 20040516 | ES 1998-945453  | 19981007   |
| US 6482841  | B1   | 20021119 | US 2000-529112  | 20000407   |
| PRIORITY APPLN. INFO.:  |      |          | CH 1997-2364    | A 19971009 |
|   |      |          | WO 1998-IB1555  | W 19981007 |

OTHER SOURCE(S): MARPAT 130:296614

AB The present invention is concerned with new pyridine double esters, their acids, and pharmaceutically acceptable salts. These compds. can be obtained by oxidation of the corresponding 1,4-dihydropyridines, and they are useful as cardioprotective agents in pharmaceutical compns. 3-O-Me 5-O-(2-tetrahydrofuranylmethyl) 2,6-dimethyl-4-phenyl-1,4-dihydropyridine-3,5-dicarboxylate, prepared in 82% yield from Me benzylideneacetoacetate and 2-tetrahydrofuranylmethyl 3-aminocrotonate, was oxidized to give 59% 3-O-Me 5-O-(2-tetrahydrofuranylmethyl) 2,6-dimethyl-4-phenylpyridine-3,5-dicarboxylate. Approx. 30 other title compds. were similarly prepared 3-O-Me 5-O-(2-tetrahydrofuranylmethyl) 2,6-dimethyl-4-(2-nitrophenyl)pyridine-3,5-dicarboxylate, prepared in 79% yield by oxidation of its 1,4-dihydro analog, gave 100% protection against death and ventricular fibrillation in rats in which coronary occlusion and reperfusion were induced.

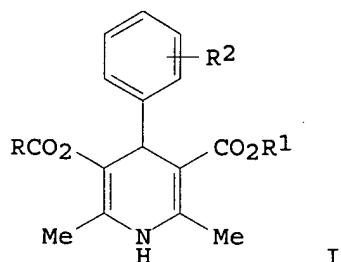
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT 85677-93-6 89267-41-4 103026-83-1  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
(preparation of cardioprotectant pyridine double esters)  
IT 100-37-8, Diethylaminoethanol 105-45-3, Methyl acetoacetate 108-01-0, Dimethylaminoethanol 447-61-0, 2-Trifluoromethylbenzaldehyde 622-40-2, 4-(2-Hydroxyethyl)morpholine 3179-63-3 7250-87-5, 1,3-Di-4-morpholinyl-2-propanol 14205-39-1, Methyl 3-aminocrotonate 15768-07-7, Methyl benzylideneacetoacetate 21829-25-4 39562-37-3, Methyl



3-cyanobenzylideneacetoacetate 67593-46-8, Methyl 2-chlorobenzylideneacetoacetate 70677-78-0 74073-22-6 90961-43-6, Methyl 3-chlorobenzylideneacetoacetate 92565-17-8 92565-18-9, 2-Tetrahydrofuranylmethyl 3-nitrobenzylideneacetoacetate 92565-37-2 102993-41-9, Methyl 3-fluorobenzylideneacetoacetate 103295-95-0, Methyl 3-trifluoromethylbenzylideneacetoacetate 103785-59-7, Methyl 2-bromobenzylideneacetoacetate 130064-42-5, 2-Tetrahydrofuranylmethyl 3-aminocrotonate 138661-03-7 157558-79-7, Methyl 3-bromobenzylideneacetoacetate 222988-50-3, 5-Oxo-2-tetrahydrofuranylmethyl 2-nitrobenzylideneacetoacetate 222988-51-4, Methyl 4-chloro-3-nitrobenzylideneacetoacetate 222988-52-5, Methyl 3-acetylaminobenzylideneacetoacetate 222988-53-6, Methyl 3-hydroxybenzylideneacetoacetate 223136-50-3 223136-52-5  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (preparation of cardioprotectant pyridine double esters)

L9 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 1991:429071 CAPLUS  
 DOCUMENT NUMBER: 115:29071  
 TITLE: Synthesis of carbon-11 labeled calcium channel antagonists  
 AUTHOR(S): Holschbach, M.; Roden, W.; Hamkens, W.  
 CORPORATE SOURCE: Inst. Med., Res. Cent. Juelich, Juelich, D-5170, Germany  
 SOURCE: Journal of Labelled Compounds and Radiopharmaceuticals (1991), 29(4), 431-42  
 CODEN: JLCRD4; ISSN: 0362-4803  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 OTHER SOURCE(S): CASREACT 115:29071  
 GI

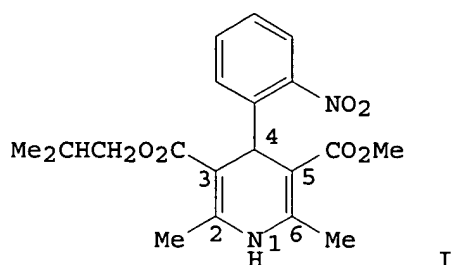


AB Dihydropyridines I [R = Me-11C; R1 = Me, R2 = 2-NO2, 2-CF3; R1 = Me2CHCH2, R2 = 2-NO2; R1 = Et, R2 = 3-NO2] were prepared by a modified Hantzsch cyclocondensation of R2C6H4CHO, MeC(NH2):CHCO2R1, and MeS(O)2CH2CH2O2CCH2C(OMe) to give 41-76% I [R = MeS(O)2CH2CH2] and sequential protective group cleavage and alkylation of the corresponding monocarboxylic acid salt with MeI-11C.  
 IT 7318-00-5, Ethyl 3-aminocrotonate 14205-39-1, Methyl 3-aminocrotonate 52937-90-3, Isobutyl 3-aminocrotonate  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (Hantzsch cyclocondensation of, with aromatic aldehydes and (methylsulfonyl)ethyl acetoacetate)  
 IT 123973-73-9P 134430-62-9P 134430-63-0P 134430-64-1P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of)

L9 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 1990:138871 CAPLUS  
 DOCUMENT NUMBER: 112:138871

10/520,066

TITLE: Syntheses of [4-carbon-14]- and [6-carbon-14]nisoldipine  
AUTHOR(S): Scherling, D.; Pleiss, U.  
CORPORATE SOURCE: Inst. Pharmacokinet., Bayer A.-G., Wuppertal, D-5600, Fed. Rep. Ger.  
SOURCE: Journal of Labelled Compounds and Radiopharmaceuticals (1988), 25(12), 1393-400  
CODEN: JLCRD4; ISSN: 0362-4803  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
OTHER SOURCE(S): CASREACT 112:138871  
GI



AB The synthesis of [4-14C]nisoldipine I starting from di-Me [14C]formamide (II) was described. II reacts with 2-O2NC6H4Li yielding 2-nitro[7-14C]benzaldehyde which on Knoevenagel condensation with iso-Bu acetoacetate yielded iso-Bu 2-(2-nitro[7-14C]benzylidene)acetoacetate (III). Key reaction step was the cyclizing Michael addition III with Me 3-aminocrotonate to give I.

IT 14205-39-1, Methyl 3-aminocrotonate  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(cyclization of, with carbon-14 labeled iso-Bu nitrobenzylideneacetylacetate)

IT 117131-06-3P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation and cyclization of, with iso-Bu nitrobenzylideneacetylacetate)

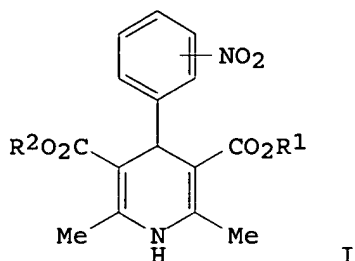
IT 125945-92-8P 125970-62-9P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of)

L9 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1989:8051 CAPLUS  
DOCUMENT NUMBER: 110:8051  
TITLE: Preparation of 4-aryl-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylates as antiangina and antihypertensive agents  
INVENTOR(S): Cupka, Pavol; Rybar, Alfonz; Svobodova, Xenia; Mahrta, Zdeno; Zlatinsky, Emil; Simko, Marian; Nevydal, Josef; Kosalko, Rudolf; Martvon, Augustin  
PATENT ASSIGNEE(S): Czech.  
SOURCE: Czech., 4 pp.  
CODEN: CZXXA9  
DOCUMENT TYPE: Patent  
LANGUAGE: Slovak  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

10/520,066

| PATENT NO.                   | KIND | DATE     | APPLICATION NO. | DATE     |
|------------------------------|------|----------|-----------------|----------|
| CS 243591                    | B1   | 19860612 | CS 1985-526     | 19850125 |
| PRIORITY APPLN. INFO.:<br>GI |      |          | CS 1985-526     | 19850125 |



AB The title compds. (I) (R1, R2 = straight or branched C1-5 alkyl, optionally interrupted with O) are prepared by reaction of MeCOCH2CO2R1 (II), (O2N)C6H4CH(O2CMe)2 (III), and MeC(NH2):CHCOR2 (IV) in an inert organic solvent at 20-150°. I are antiangina and antihypersensitive agents (no data). A mixture of 2-(O2N)C6H4CH(O2CMe)2 7.54 g, II (R1 = Me) 4 mL, IV (R2 = Me) 4.1 g, and MeOH 10 mL was refluxed 7 h, cooled, and filtered to obtain a crude product which was recrystd. from EtOAc to give 65% I (R1, R2 = Me; NO2 in 2-position).

IT 14205-39-1

RL: RCT (Reactant); RACT (Reactant or reagent)  
(cyclocondensation of, with Me acetoacetate and nitrobenzaldehyde diacetate)

|    |             |             |             |             |             |
|----|-------------|-------------|-------------|-------------|-------------|
| IT | 21829-09-4P | 21829-10-7P | 21829-25-4P | 21829-26-5P | 21829-27-6P |
|    | 21829-28-7P | 21881-54-9P | 21881-77-6P | 21881-78-7P | 22609-70-7P |
|    | 22609-71-8P | 22609-72-9P | 22609-73-0P | 39562-18-0P | 39562-70-4P |
|    | 63675-72-9P |             |             |             |             |

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of, as antiangina and antihypertensive agent)

L9 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1988:55851 CAPLUS

DOCUMENT NUMBER: 108:55851

TITLE: Crystal structures and pharmacologic activities of 1,4-dihydropyridine calcium channel antagonists of the isobutyl methyl 2,6-dimethyl-4-(substituted phenyl)-1,4-dihydropyridine-3,5-dicarboxylate (nisoldipine) series

AUTHOR(S): Fossheim, R.; Joslyn, A.; Solo, A. J.; Luchowski, E.; Rutledge, A.; Triggle, D. J.

CORPORATE SOURCE: Dep. Chem., Univ. Oslo, Oslo, 0315, Norway

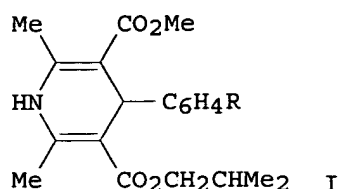
SOURCE: Journal of Medicinal Chemistry (1988), 31(2), 300-5  
CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 108:55851

GI



AB Nine racemic iso-Bu Me 2,6-dimethyl-4-aryl-1,4-dihydropyridine-3,5-dicarboxylates (I; R = H, 2-NO<sub>2</sub>, 3-NO<sub>2</sub>, 3-cyano, 3-OMe, 4-F, 2-CF<sub>3</sub>, 3-CF<sub>3</sub>, 4-Cl) including nisoldipine (R = 2-NO<sub>2</sub>) were prepared and evaluated as Ca channel antagonists against binding of nitrendipine tritiated in the methoxy group and K<sup>+</sup>-depolarization-induced tension responses in intestinal smooth muscle. The x-ray crystal structures of I (R = H, 2-NO<sub>2</sub>, 3-NO<sub>2</sub>, 3-cyano, 3-OMe, 4-F) were determined. The degree of 1,4-dihydropyridine ring puckering depends on the nature and position of the Ph substituent and the inter-ring conformation. Different ester substituents affect the ring puckering to a small extent in most cases. Pharmacol. and radioligand binding activities for the 9 compds. studied show a parallel dependence on the Ph substituent, but the compds. are .apprx.10 times more active in the radioligand binding assay than in the pharmacol. assay. Pharmacol. activity increases with increasing dihydropyridine ring planarity.

IT 14205-39-1

RL: RCT (Reactant); RACT (Reactant or reagent)  
(Hantzsch reaction of, with iso-Bu acetoacetate and  
(trifluoromethyl)benzaldehydes, dihydropyridines from)

IT 63675-72-9P, (+)-Nisoldipine 111556-83-3P 111556-84-4P  
111556-85-5P 111556-86-6P 113578-26-0P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation, mol. structure, calcium channel antagonistic activity, and  
nitrendipine binding inhibition of)

L9 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1987:4897 CAPLUS

DOCUMENT NUMBER: 106:4897

TITLE: Isobutyl 2,6-dimethyl-3-methoxycarbonyl-4-(2-nitrophenyl)-1,4-dihydropyridine-5-carboxylate

INVENTOR(S): Sune Coma, Nuria

PATENT ASSIGNEE(S): Spain

SOURCE: Span., 9 pp.

CODEN: SPXXAD

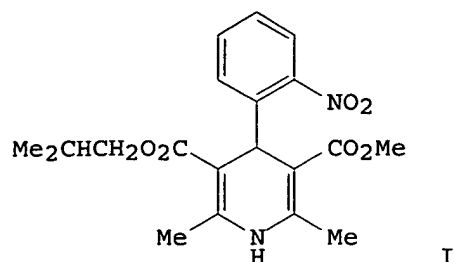
DOCUMENT TYPE: Patent

LANGUAGE: Spanish

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO.             | KIND | DATE     | APPLICATION NO. | DATE     |
|------------------------|------|----------|-----------------|----------|
| -----                  | ---- | -----    | -----           | -----    |
| ES 546784              | A1   | 19860101 | ES 1985-546784  | 19850909 |
| PRIORITY APPLN. INFO.: |      |          | ES 1985-546784  | 19850909 |
| GI                     |      |          |                 |          |



AB Title compound I was prepared as follows. A mixture of 2-O<sub>2</sub>NC<sub>6</sub>H<sub>4</sub>CH(OAc)<sub>2</sub>, Me<sub>2</sub>CHCH<sub>2</sub>O<sub>2</sub>CCH<sub>2</sub>COMe, and Me(H<sub>2</sub>N)C:CHCO<sub>2</sub>Me in EtOH-pyridine was refluxed for 7 h to give 58% I.

IT 14205-39-1, Methyl 3-aminocrotonate

RL: RCT (Reactant); RACT (Reactant or reagent)  
(cyclocondensation of, with acetoacetate and nitrobenzaldehyde diacetate)

IT 63675-72-9P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of, by cyclocondensation of acetoacetate, aminocrotonate, and nitrobenzaldehyde diacetate)

L9 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1984:156503 CAPLUS

DOCUMENT NUMBER: 100:156503

TITLE: Use of 1,4-dihydropyridines as antiarteriosclerotics

INVENTOR(S): Seuter, Friedel; Bossert, Friedrich; Meyer, Horst;  
Wehinger, Egbert; Boeshagen, Horst

PATENT ASSIGNEE(S): Bayer A.-G., Fed. Rep. Ger.

SOURCE: Ger. Offen., 14 pp.

CODEN: GWXXBX

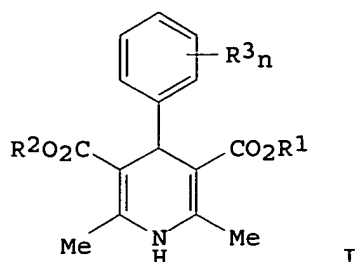
DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO.             | KIND | DATE     | APPLICATION NO. | DATE       |
|------------------------|------|----------|-----------------|------------|
| -----                  | ---- | -----    | -----           | -----      |
| DE 3222367             | A1   | 19831215 | DE 1982-3222367 | 19820615   |
| DE 3222367             | C2   | 19920213 |                 |            |
| JP 59005114            | A2   | 19840112 | JP 1983-103003  | 19830610   |
| JP 05053774            | B4   | 19930810 |                 |            |
| BE 897035              | A1   | 19831213 | BE 1983-210988  | 19830613   |
| CA 1228549             | A1   | 19871027 | CA 1983-430227  | 19830613   |
| FR 2528425             | A1   | 19831216 | FR 1983-9798    | 19830614   |
| FR 2528425             | B1   | 19870206 |                 |            |
| ES 523244              | A1   | 19840316 | ES 1983-523244  | 19830614   |
| ZA 8304344             | A    | 19840328 | ZA 1983-4344    | 19830614   |
| PRIORITY APPLN. INFO.: |      |          | DE 1982-3222367 | A 19820615 |
| GI                     |      |          |                 |            |



AB Dihydropyridines I [R1, R2 = C1-12 alkyl or alkoxyalkyl, alkyl (un)substituted with Cl or F; R3 = NO2, CF3, halo, cyano; n = 1,2], useful as antiatherosclerotics or in treating arteriosclerosis, were prepared by boiling 3-O<sub>2</sub>NC<sub>6</sub>H<sub>4</sub>CH:C(CO<sub>2</sub>Et)CO<sub>2</sub>Me and H<sub>2</sub>NCMe:CHCO<sub>2</sub>Me in EtOH 10 h gave 67% I (R1 = Me, R2 = Et, R3n = 3-NO<sub>2</sub>), which reduced arteriosclerotic plaque in rat arteries by 49% at 30 mg/kg orally.

IT 14205-39-1 52937-92-5

RL: RCT (Reactant); RACT (Reactant or reagent)  
(cyclization of, with Et (nitrobenzylidene)acetoacetate, dihydropyridinedicarboxylate by)

IT 22609-73-0P 63675-72-9P 88284-22-4P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of, as antiarteriosclerotic)

L9 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1977:484831 CAPLUS

DOCUMENT NUMBER: 87:84831

TITLE: Isobutyl 2,6-dimethyl-3-methoxycarbonyl-4-(2-nitrophenyl)-1,4-dihydropyridine-5-carboxylate with coronary therapeutic action

INVENTOR(S): Wehinger, Egbert; Bossert, Friedrich; Heise, Arend; Kazda, Stanislav; Stoepel, Kurt; Vater, Wulf

PATENT ASSIGNEE(S): Bayer A.-G., Fed. Rep. Ger.

SOURCE: Ger. Offen., 19 pp.

CODEN: GWXXBX

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

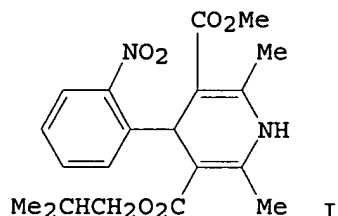
PATENT INFORMATION:

| PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE     |
|-------------|------|----------|-----------------|----------|
| -----       | ---- | -----    | -----           | -----    |
| DE 2549568  | A1   | 19770518 | DE 1975-2549568 | 19751105 |
| DE 2549568  | B2   | 19800821 |                 |          |
| DE 2549568  | C3   | 19811029 |                 |          |
| NO 7603608  | A    | 19770506 | NO 1976-3608    | 19761022 |
| NO 145574   | B    | 19820111 |                 |          |
| NO 145574   | C    | 19820421 |                 |          |
| JP 52059161 | A2   | 19770516 | JP 1976-129540  | 19761029 |
| JP 56047185 | B4   | 19811107 |                 |          |
| IL 50817    | A1   | 19790725 | IL 1976-50817   | 19761102 |
| CS 200499   | P    | 19800915 | CS 1976-7068    | 19761102 |
| CH 623038   | A    | 19810515 | CH 1976-13819   | 19761102 |
| RO 70295    | P    | 19810817 | RO 1976-88294   | 19761102 |
| FI 7603160  | A    | 19770506 | FI 1976-3160    | 19761103 |
| FI 60704    | B    | 19811130 |                 |          |
| FI 60704    | C    | 19820310 |                 |          |
| NL 7612198  | A    | 19770509 | NL 1976-12198   | 19761103 |
| NL 175915   | B    | 19840816 |                 |          |
| NL 175915   | C    | 19850116 |                 |          |

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|                        |    |          |                 |             |
|------------------------|----|----------|-----------------|-------------|
| AT 352129              | B  | 19790910 | AT 1976-8142    | 19761103    |
| AT 7608142             | A  | 19790215 |                 |             |
| PL 106084              | P  | 19791130 | PL 1976-193438  | 19761103    |
| PL 105940              | P  | 19791130 | PL 1976-201800  | 19761103    |
| BE 847968              | A1 | 19770504 | BE 1976-172063  | 19761104    |
| DK 7604984             | A  | 19770506 | DK 1976-4984    | 19761104    |
| DK 146762              | B  | 19831227 |                 |             |
| DK 146762              | C  | 19840612 |                 |             |
| SE 7612308             | A  | 19770506 | SE 1976-12308   | 19761104    |
| SE 423542              | B  | 19820510 |                 |             |
| SE 423542              | C  | 19820819 |                 |             |
| ZA 7606622             | A  | 19771026 | ZA 1976-6622    | 19761104    |
| CA 1085406             | A1 | 19800909 | CA 1976-264921  | 19761104    |
| FR 2330395             | A1 | 19770603 | FR 1976-33488   | 19761105    |
| FR 2330395             | B1 | 19781222 |                 |             |
| AU 498964              | B2 | 19790329 | AU 1976-19358   | 19761105    |
| AU 7619358             | A1 | 19780511 |                 |             |
| CS 200500              | P  | 19800915 | CS 1977-6535    | 19771007    |
| US 4154839             | A  | 19790515 | US 1978-903573  | 19780508    |
| CH 622779              | A  | 19810430 | CH 1980-5678    | 19800724    |
| PRIORITY APPLN. INFO.: |    |          | DE 1975-2549568 | A 19751105  |
|                        |    |          | CH 1976-13819   | A 19761102  |
|                        |    |          | CS 1976-7068    | 19761102    |
|                        |    |          | US 1976-738383  | A1 19761102 |

GI



AB The title compound (I) was prepared in 78% yield by treating 2-O<sub>2</sub>NC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>C(OMe)CO<sub>2</sub>CH<sub>2</sub>CHMe<sub>2</sub> with H<sub>2</sub>NCMe:CHCO<sub>2</sub>Me. At 0.003 mg/kg sublingually in dogs I increased the myocardial blood flow by 23% with a halflife of 100 min.

IT 14205-39-1 52937-90-3

RL: RCT (Reactant); RACT (Reactant or reagent)  
(condensation of, with nitrobenzylideneacetoacetate)

IT 63675-72-9P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation and cardiac activity of)

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FILE 'USPATFULL' ENTERED AT 09:49:59 ON 13 DEC 2005

CA INDEXING COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'USPAT2' ENTERED AT 09:49:59 ON 13 DEC 2005

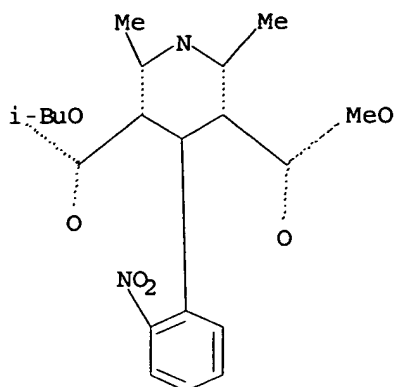
CA INDEXING COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY (ACS)

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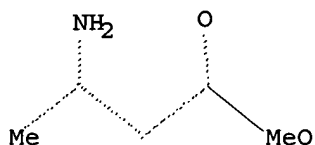
L4

STR

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Structure attributes must be viewed using STN Express query preparation.  
L5 STR



Structure attributes must be viewed using STN Express query preparation.

L6 21 SEA FILE=REGISTRY SSS FUL L4  
L7 315 SEA FILE=REGISTRY SSS FUL L5  
L10 3 SEA L6 AND L7

=> d l10 ibib abs hit

L10 ANSWER 1 OF 3 USPATFULL on STN

ACCESSION NUMBER: 2005:275457 USPATFULL

TITLE: Industrial process for the synthesis of isobutyl methyl  
1,4-dihydro-2,6-dimethyl-4-(2-nitrophenyl)-3,5-pyridine  
dicarboxylate (nisoldipine)

INVENTOR(S): Ferrari, Massimo, Cenate Sotto, ITALY  
Ghezzi, Marcello, Curno, ITALY  
Alberelli, Manuel, Casazza, ITALY  
Ambrosini, Alberto, Lallio, ITALY

|                     | NUMBER         | KIND | DATE                  |
|---------------------|----------------|------|-----------------------|
| PATENT INFORMATION: | US 2005240022  | A1   | 20051027              |
| APPLICATION INFO.:  | US 2003-520066 | A1   | 20030626 (10)         |
|                     | WO 2003-EP6755 |      | 20030626              |
|                     |                |      | 20050103 PCT 371 date |

|                       | NUMBER  | DATE |
|-----------------------|---|------|
| PRIORITY INFORMATION: | IT 2003-MI200200144520020701  |      |
| DOCUMENT TYPE:        | Utility   |      |
| FILE SEGMENT:         | APPLICATION   |      |
| LEGAL REPRESENTATIVE: | GIFFORD, KRASS, GROH, SPRINKLE & CITKOWSKI, P.C, PO BOX<br>7021, TROY, MI, 48007-7021, US |      |
| NUMBER OF CLAIMS:     | 15  |      |
| EXEMPLARY CLAIM:      | 1   |      |
| LINE COUNT:           | 222   |      |



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CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Synthetic process of isobutyl methyl 1,4-dihydro-2,6-dimethyl-4-(2-nitrophenyl)3,5-pyridine dicarboxylate (Nisoldipine) comprising on the reaction of isobutyl 2-(2-nitrobenzylidene)acetoacetate with methyl 3-aminocrotonate in an apolar solvent.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 552-89-6, 2-Nitrobenzaldehyde 7779-75-1, Isobutyl acetoacetate 14205-39-1, Methyl 3-aminocrotonate (synthesis of nisoldipine by the reaction of iso-Bu 2-(2-nitrobenzylidene)acetoacetate with Me 3-aminocrotonate)

IT 63675-72-9P, Nisoldipine (synthesis, by the reaction of iso-Bu 2-(2-nitrobenzylidene)acetoacetate with Me 3-aminocrotonate)

=> d l10 2-3 ibib abs hit

L10 ANSWER 2 OF 3 USPATFULL on STN

ACCESSION NUMBER: 2002:304006 USPATFULL

TITLE: Pyridyl compounds and pharmaceutical compositions containing them

INVENTOR(S): Letelier, Carlos Sunkel, Madrid, SPAIN  
Munoz, Miguel Fau De Casa-Juana, Madrid, SPAIN  
Gomez, Julio Alvarez-Builla, Madrid, SPAIN  
Ortega, Jose M. Minguez, Madrid, SPAIN  
Statkow, Pierre, Geneva, SWITZERLAND  
Straumann, Danielle, Martigny, SWITZERLAND  
Chatterjee, Shyam S., Karlsruhe, GERMANY, FEDERAL REPUBLIC OF

PATENT ASSIGNEE(S): Cermol S.A., Evionnaz, SWITZERLAND (non-U.S. corporation)

|                     | NUMBER         | KIND | DATE                  |
|---------------------|----------------|------|-----------------------|
| PATENT INFORMATION: | US 6482841     | B1   | 20021119              |
|                     | WO 9919302     |      | 19990422              |
| APPLICATION INFO.:  | US 2000-529112 |      | 20000407 (9)          |
|                     | WO 1998-IB1555 |      | 19981007              |
|                     |                |      | 20000407 PCT 371 date |

|                       | NUMBER                                 | DATE     |
|-----------------------|--|----------|
| PRIORITY INFORMATION: | CH 1997-2364                           | 19971009 |
| DOCUMENT TYPE:        | Utility                                |          |
| FILE SEGMENT:         | GRANTED                                |          |
| PRIMARY EXAMINER:     | Rotman, Alan L.                        |          |
| ASSISTANT EXAMINER:   | Desai, Rita                            |          |
| LEGAL REPRESENTATIVE: | Young & Thompson                       |          |
| NUMBER OF CLAIMS:     | 6                                      |          |
| EXEMPLARY CLAIM:      | 1                                      |          |
| NUMBER OF DRAWINGS:   | 0 Drawing Figure(s); 0 Drawing Page(s) |          |
| LINE COUNT:           | 1042                                   |          |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB ##STR1##

The present invention is concerned with new pyridine double esters of formula (I), their acids, and pharmaceutically acceptable salts. These compounds can be obtained by oxydation of the corresponding 1,4-dihydropyridines, and they are useful as cardioprotective agents in pharmaceutical compositions.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 85677-93-6 89267-41-4 103026-83-1  
 (preparation of cardioprotectant pyridine double esters)  
 IT 100-37-8, Diethylaminoethanol 105-45-3, Methyl acetoacetate 108-01-0,  
 Dimethylaminoethanol 447-61-0, 2-Trifluoromethylbenzaldehyde  
 622-40-2, 4-(2-Hydroxyethyl)morpholine 3179-63-3 7250-87-5,  
 1,3-Di-4-morpholinyl-2-propanol 14205-39-1, Methyl  
 3-aminocrotonate 15768-07-7, Methyl benzylideneacetoacetate  
 21829-25-4 39562-37-3, Methyl 3-cyanobenzylideneacetoacetate  
 67593-46-8, Methyl 2-chlorobenzylideneacetoacetate 70677-78-0  
 74073-22-6 90961-43-6, Methyl 3-chlorobenzylideneacetoacetate  
 92565-17-8 92565-18-9, 2-Tetrahydrofuranylmethyl 3-  
 nitrobenzylideneacetoacetate 92565-37-2 102993-41-9, Methyl  
 3-fluorobenzylideneacetoacetate 103295-95-0, Methyl  
 3-trifluoromethylbenzylideneacetoacetate 103785-59-7, Methyl  
 2-bromobenzylideneacetoacetate 130064-42-5, 2-Tetrahydrofuranylmethyl  
 3-aminocrotonate 138661-03-7 157558-79-7, Methyl 3-  
 bromobenzylideneacetoacetate 222988-50-3, 5-Oxo-2-  
 tetrahydrofuranylmethyl 2-nitrobenzylideneacetoacetate 222988-51-4,  
 Methyl 4-chloro-3-nitrobenzylideneacetoacetate 222988-52-5, Methyl  
 3-acetylaminobenzylideneacetoacetate 222988-53-6, Methyl  
 3-hydroxybenzylideneacetoacetate 223136-50-3 223136-52-5  
 (preparation of cardioprotectant pyridine double esters)

## L10 ANSWER 3 OF 3 USPATFULL on STN

ACCESSION NUMBER: 79:24268 USPATFULL

TITLE: 2,6-Dimethyl-3-carboxymethoxy-4-(2-nitrophenyl)-5-  
carbisobutoxy-1,4-dihydropyridine

INVENTOR(S): Wehinger, Egbert, Velbert, Germany, Federal Republic of  
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 PATENT ASSIGNEE(S): Bayer Aktiengesellschaft, Germany, Federal Republic of  
 (non-U.S. corporation)

|                       | NUMBER  | KIND | DATE         |
|-----------------------|---|------|--------------|
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| RELATED APPLN. INFO.: | Continuation of Ser. No. US 1976-738383, filed on 2 Nov 1976, now abandoned |      |              |

|                       | NUMBER          | DATE     |
|-----------------------|-----------------|----------|
| PRIORITY INFORMATION: | DE 1975-2549568 | 19751105 |
| DOCUMENT TYPE:        | Utility         |          |
| FILE SEGMENT:         | Granted         |          |
| PRIMARY EXAMINER:     | Rotman, Alan L. |          |
| LEGAL REPRESENTATIVE: | Jacobs & Jacobs |          |
| NUMBER OF CLAIMS:     | 5               |          |
| EXEMPLARY CLAIM:      | 1               |          |
| LINE COUNT:           | 246             |          |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The isobutyl methyl 1,4-dihydro-2,6-dimethyl-4-(2-nitrophenyl)-3,5-  
 pyridinedicarboxylate demonstrates the unique ability of increasing  
 myocardial perfusion upon oral or intravenous administration. Methods of  
 preparing the compound, its use in coronary conditions and  
 pharmaceutical compositions for effecting that use are disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

10/520,066

IT 14205-39-1 52937-90-3

(condensation of, with nitrobenzylideneacetoacetate)

IT 63675-72-9P

(preparation and cardiac activity of)

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